Epidemiology for the Uninitiated

Comparing rates

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"Is this disease increasing? Does it occur with undue frequency in my local community? Does its incidence correlate with some hypothesised cause? Has the outcome changed since control measures were instituted?" To answer such questions means setting two sets of rates side by side and making some sense of the comparison. This article will examine some of the problems which may arise.

Terminology and classification of diseases

Diagnostic labels and groupings are many and various, and in continual flux: in the interests of communication some standardisation is necessary, even though no single system can meet all requirements.

THE ICD SYSTEM

The *International Classification of Diseases, Injuries, and Causes of Death*, published by the World Health Organisation, assigns a 3-digit numerical code to every major condition. Often a fourth digit is added for more exact specification: for example, ICD 204 is "lymphatic leukaemia," which may additionally be specified as 204.0 "acute" or 204.1 "chronic." Broader groupings are readily formed—for example, ICD 200-209 consists of all neoplasms of lymphatic and haematopoietic tissue. This system is used for coding death certificates. It determines the presentation of results in the Registrar General's reports, and in the diagnostic registers of most hospitals.

Periodically, the system has to be revised to keep pace with medical usage. The new (9th) revision comes into general use in 1979—consequently, some rates published before and after this year will not be directly comparable.

In interpreting time trends it is also essential to consider changes in diagnostic standards and clinical terminology. Historical epidemiology is a dangerous pursuit, but errors are less likely if the analysis deals in broad disease categories. For example, coronary heart disease mortality rates in American men declined between 1968 and 1974 by 22%. One explanation for this might be that deaths formerly attributed to this cause are now being called something else (hypertension, cardiomyopathy, or viral myocarditis). The case for a real decline is much strengthened by finding that the trend applies also to "all cardiovascular diseases," and even to total (all-causes) mortality.

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Confounding variables

In an ideal laboratory experiment the investigator alters only one variable at a time, so that any effect he observes can only be due to that variable: all associations are causal. Studying human disease is quite different. Most epidemiological studies are observational, not experimental, and compare people who differ in all kinds of ways, known and unknown. Analytic epidemiology is concerned with the attempt to isolate the effect of one key factor from among a tangled mass of confounding variables, any of which might explain the observed result.

According to the Hospital In-patient Enquiry the case fatality ratio for acute coronary heart disease is higher in women (27%) than in men (21%). This is a statement of fact: the problem comes in its interpretation. Does female sex as such adversely affect prognosis, or is the result due to some confounding variable such as age? Simple cross-classification (table I) produces a surprising result. The crude (all ages) rate is higher in women, and yet no real difference is seen within any individual age class. Age powerfully influences fatality, whereas sex as such has no effect at all; the crude rate is misleading simply because a higher proportion of the women patients come from the older, higher risk ages. This leads to a basic rule of epidemiological analysis: "*Crude rates must never be used to compare populations of different structure.*"

TABLE I—*Case fatality for acute coronary heart disease in hospital admissions*

Age (years)	Case fatality ratio (%) (and No of patients)	
	Men	Women
15-44	5 (6300)	3 (1200)
45-64	13 (45 600)	14 (13 700)
≥65	36 (31 800)	35 (27 700)
Total	21	27

Crude rates are not false but they are often misleading, because they fail to take into account other variables, particularly age. Every epidemiological report should describe the age structure of its study group and take account of it in the analysis. Cross-tabulation is the simplest solution, and yields *age-specific rates.*

In England and Wales the age-specific all-causes mortality rate for men aged 65-74 has not changed appreciably in the last 30 years, despite the great amount of medication that they now consume. This is a valid comparison of rates, even though there have been big changes in the age structure of the whole population and the proportion of the elderly.

The method of cross-classification and class-specific rates is theoretically able to cope with multiple variables. In a study of bronchitis, for example, the prevalence (%) of persistent cough and phlegm could be cross-tabulated by sex, age, and number of cigarettes smoked:

Age (years)	Sex	No of cigarettes/day			
		0	<20	20	>20
35-44	M	1·3	3·7	8·6	17·5
	F	1·5	2·9	7·0	15·7
45-54	M	..	..	..	..
..	..	..	..	..	..
..	..	..	..	..	..

The limitations to this approach are the indigestibility of large tables and lack of numbers: most surveys are too small to examine all the interesting subgroups.

Standardised rates

In place of a cumbersome array of class-specific rates one would often prefer the convenience of a single number to summarise the position after taking account of age and other factors. *Standardised* or *adjusted rates* provide for this need. Two techniques are available.

DIRECT STANDARDISATION

In the USA over the last 10 years deaths from coronary heart disease are said to have been declining in all age groups. How can the overall trend be summarised? Crude rates cannot be used, because the population's age structure has changed. Direct standardisation includes a *weighted average* of the age-specific rates in each year, with weights equal to the proportion of persons in each age group in a convenient reference population (for example, the whole nation in the mid-point of the period). For men in 1968 the procedure is as shown in table II.

TABLE II—*Example of direct standardisation*

Age (years)	CHD deaths/100 000 (1)	% Of reference population in age group (2)	(1) × (2)
35-44	93	34·4	3 199·2
45-54	355	36·0	12 780·0
55-64	961	29·5	28 349·5
Total		100	44 328·7 ÷ 100 = 443

Table III shows the standardised rates for men and women in the ensuing years, calculated in the same way. They show a remarkable fall.

INDIRECT STANDARDISATION

The direct method is for large studies, and in most surveys the indirect method yields more stable risk estimates. Suppose that a general practitioner wants to test his impression of a local excess of chronic bronchitis. Using a standard questionnaire, he examines a sample of middle-aged men from his list, and finds that 45 have persistent cough and phlegm. Is this excessive? His calculation is shown in table IV.

TABLE III—*Coronary heart disease in USA (ages 35-64): changes in age-standardised mortality rates (deaths/100 000/year)*

	1968	1969	1970	1971	1972	1973	1974
Men	443	430	420	413	408	399	377
Women	134	126	126	124	120	118	111

TABLE IV—*Example of indirect standardisation*

Age (years)	No in study (1)	Symptom prevalence in reference group (2)	Expected cases = (1) × (2)
35-44	150	8%	12
45-54	100	9%	9
55-64	90	10%	9
Total			30

First he sets out the number of subjects in each age class (column 1). He must then choose a suitable reference population in which the class-specific rates are known (column 2). (In mortality studies this would usually be the nation or some subset of it, such as a particular region or social class; in multicentre studies it could be the pooled data from all centres.) Cross-multiplying columns 1 and 2 for each class gives the expected *number* of cases in a group of that age and size, based on the reference population's rates. Summation over all classes gives the total expected frequency, given the size and age structure of that particular study. Where 30 cases were expected he has observed 45, giving an age-adjusted *relative risk or standardised prevalence ratio* of 45/30 = 150%.

A comparable statistic, the *standardised mortality ratio* (SMR) is widely used by the Registrar General in summarising time trends and occupational differences. Thus in 1971 the SMR for death by accidents in doctors was 180%, indicating a large excess relative to the population at the time. To analyse time trends, as with the cost-of-living index, an arbitrary base year is taken.

OTHER STANDARDISATION TECHNIQUES

Life expectation is an age-adjusted summary of current all-causes mortality, being the average number of years that an individual would expect to live if exposed to the current age-specific rates. More tedious to calculate than an SMR, its meaning is more evident. Thus the current life expectation for men in the north-west region of England and Wales is only 67·9 years, compared with 71·3 years in East Anglia.

Regression techniques are an efficient means of standardisation and, thanks to computers, they are increasingly popular. The regression line relating ventilatory function to age, for example, may be used in a survey to correct each man's value to what would be expected at, say, age 40. Subsequent analysis employs these age-corrected values. In *multivariate analysis* a computer, using regression or similar methods, can standardise for variables simultaneously. Powerful though they are, these new techniques have by no means displaced the simpler and more robust methods of cross-tabulation.

Eventually this series will be collected into a book and hence no reprints will be available from the authors.

Is laryngeal spasm with inspiratory stridor a common occurrence in adult patients with laryngotracheitis?

Laryngeal spasm with inspiratory stridor is not common in adult patients with laryngotracheitis. Some patients, especially asthmatic patients, develop considerable "wheeze," which may be as severe on inspiration as expiration. Others may get transient inspiratory stridor and spasm after coughing fits. If inspiratory stridor persists it should be investigated in more detail.